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PSEUDO-HYPERTROPHIC MUSCULAR ATROPHY.

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I. INTRODUCTION.

Cases of muscular atrophy may be of at least three distinct types, viz.: (1) those due to lesions in the central nervous system; (2) those due to lesions in the peripheral nerves; and (3) those due to a primary lesion of the muscles themselves. The last of these forms is also spoken of as a muscular dystrophy; and as the case here reported is of this form, it may be of interest to see how this type is defined. I quote here Dr. Osler's[1] definition. He says that it is a "muscular wasting, with or without an initial hypertrophy, beginning in various groups of muscles, usually progressive in character, and dependent on primary changes in the muscles themselves." Pseudo-hypertrophic Muscular Atrophy is that form of muscular dystrophy which affects infants, which is preceded by a pseudo-hypertrophy and, which attacks first the muscles of the calves of the legs.

II. HISTORICAL STATEMENT.

The first cases of muscular atrophy mentioned in the literature upon this subject were studied with no reference to the microscopical condition of the spinal cord, the peripheral nerves, or of the muscles themselves. The diagnosis was based entirely on the history and on the clinical findings in the case; nor was any serious attempt made to find the real cause of the various symptoms that were observed. Thus Bell (1830),[2] though he made no microscopical examination of the tissues, was the first investigator to describe such cases of muscular atrophy as have of late been called Pseudo-hypertrophic Muscular Atrophy. In 1836 he made the first clinical description of a case of Progressive Spinal Paralysis. Aran (1850)[3] was the first investigator to demonstrate changes in the spinal cord of cases of Progressive Spinal Paralysis, while Meryon (1852)[4] was the first to demonstrate that in cases of Pseudo-hypertrophic Muscular Atrophy no microscopical changes are present in the spinal cord, but that the muscles had undergone a "fatty and granular degeneration."

Duchenne (1868)[5] also recognized that this disease is independent of all changes in the central nervous system and gave it the name "Pseudo-hypertrophic Muscular Atrophy."

Charcot (1872)[6] discovered Amyotrophic Lateral Sclerosis, and pointed out the differences between it and Progressive Spinal Mucular Atrophy. Friedreich (1873)[7] discussed fully the reasons for separating the muscular dystrophies from the forms of spinal muscular atrophy. Dejerine (1882) and others, showed that numerous cases formerly supposed to be due to spinal lesion were really due to multiple neuritis. Erb (1882)[8] described the form of muscular dystrophy which he called "juvenile," and later (1884)[9] gave a full account of the same. Landouzy and Dejerine (1884) described the facio-scapulo-humeral form of muscular dystrophy, and later (1885)[10] gave a more extended discussion of the same. Gowers (1879)[11] collected and studied 160 cases of Pseudo-hypertrophic Muscular Dystrophy, and more than 140 cases have been reported, by various writers, since the publishing of his paper. Concerning the condition of the spinal cord in this disease, Gowers (1899)[12] wrote: "The motor nerves, when examined, have been found normal. The spinal cord has been found perfectly normal in most cases in which it has been examined . . ., the anterior gray matter was unaffected. Hemorrhages have been occasionally found. The neuroglia cells have been found increased in number."

III. CLASSIFICATION.

It is therefore evident that the forms of muscular atrophy may well be arranged into three groups:

(a) Those due to changes in the spinal cord: Progressive Spinal Muscular Atrophy, etc.

(b) Those due to changes in the peripheral nerves: Multiple Neuritis, Progressive Neural Muscular Atrophy, etc.

(c) Those due to primary changes in the muscles: The muscular dystrophies.

Erb (1891)[13] has classified the forms of muscular dystrophies as follows:

I. Dystrophia Muscularis Progressiva Infantum.
    1. Hypertrophic form,
        a. With pseudo-hypertrophy or lipomatosis, Duchenne's Pseudo-hypertrophic Muscular Atrophy.
        b. With real hypertrophy.
    2. Atrophic form,
        a. With primary involvement of the face (Duchenne's infantile form or the Landouzy-Dejerine type).
        b. Without involvement of the face.

II. Dystrophia Muscularis Progressiva Juvenum vel Adulterum (Erb's juvenile form).

According to another classification the types of the disease and the muscle-groups affected are as follows:

1. Duchenne's pseudo-hypertrophy,—muscles of calves of legs.
2. Erb's juvenile dystrophy,—muscles of arms and shoulders.
3. Sachs'-Hoffmann type,—peroneal muscles of legs.
4. Landouzy-Dejerine type,—muscles of face and arms.
5. Charcot-Marie-Tooth type,—muscles of forearms, legs, and back.

The above classifications are given in order that the reader may be better able to place the case here reported.

IV. CLINICAL HISTORY OF THE CASE REPORTED.

His mother, as well as his paternal grandfather died of cancer. One of his sisters was still-born, and a brother shows neurotic tendencies. An aunt on his father's side has been confined in an insane asylum. A cousin is said to have had cerebro-spinal meningitis leaving one leg crippled. There is no history of any other case of Pseudo-hypertrophic Muscular Atrophy among his ancestors or relatives.

The following communication from the boy's father seems to be of sufficient importance to warrant its insertion. He says:

"I do not know that he was ever sick with any disease before the onset of the trouble with his feet."—"I don't remember the two days'sleeping spell to which you refer. The child did have a seeming desire to be held and acted sort of droopy and whined when not asleep as if in pain, and this lasted the greater part of three months, I think. This was before anything wrong was noticed about his ankles, and it was in his ankles that the trouble made its first appearance. As I think I stated in the other letter, for quite a long while the trouble was so slight that we thought little of it. All the physicians consulted, and they were not a few, made light of the trouble. They said it was nothing worthy of notice. To me it seemed many times that the calves of the boy's legs were large, and a great deal of the time were devoid of feeling. For instance, one night when we were living in Tacoma, Wash., a lot of children went out coasting on the hill and took this boy with them. As he could not walk, they hauled him up the hill on the sled, and when they came in, the calves of his legs were nearly frozen without his knowing it. He was then nine years old."

The first abnormality noticed was his going on all fours, using the sides of his feet, when moving about on the floor. He began to walk before he was two years old, but never learned to walk well. He stumbled and fell frequently, as he was unable to flex dorsally either his toes or his feet. When about six years old he wore a brace for a short time. At ten, he found it necessary to use a cane while walking; and at twelve, crutches. He was always frail and this became more apparent as he grew older. He was, however, intelligent and very fond of reading. His arms seemed normal as regards strength, but the movements of his hands were both slow and clumsy. When about twelve years of age he experienced, occasionally, a difficulty in retaining the contents of his rectum, though he was able to perceive the inclination to evacuate his bowels. He seemed normally developed sexually, and never had any trouble in retaining the contents of the bladder. Especially since twelve years of age, have the calves of his legs been abnormally thin. He had always considerable difficulty in going up stairs, and frequently lost his balance. Except when very young, only the balls of his feet touched the ground while walking. He was able to remain in a sitting posture with no difficulty; but was unable to arise from this position without assisting himself with his hands. In arising from the prone position he would first roll over on his face, get up on his hands and knees, then on all fours, and finally raise his trunk by putting his hands on his knees. He showed a lessened sensibility to cold in his feet and in the calves of his legs, though the other sensations were apparently normal. In the later years of his life his shoulder-blades were rather prominent; but this was, no doubt, partly due to the emaciated condition in which he then was. He had attacks of both measles and whooping-cough, but not until after the onset of his trouble.

The immediate cause of his death was an attack of typhoid fever, which lasted six or seven weeks. During this attack he was in the St. Luke's Hospital, Chicago, where he died February 24, 1903, at the age of twenty years.

(The above history has been obtained from friends and relatives since the death of the patient.)

V. POST MORTEM EXAMINATION.

This was made by Dr. H. G. Wells (1903),[14] Chicago, and showed the following conditions present:

"Anatomical Diagnosis.—Extreme emaciation; typhoid ulceration of the colon; hypertrophic pulmonary emphysema; purulent bronchitis; bronchopneumonia; hypostatic pneumonia of left lung; edema of the right lower lobe of lung; acute lymphadenitis, peribronchial and mesenteric; hyperplasia of the aorta; hypertrophy of the left ventricle of the heart; parenchymatous degeneration of the liver and the kidneys; fibrous pericholecystitis; atrophy of appendix vermiformis; hyperplasia of the spleen; omentum almost devoid of fat; calcification of the peripancreatic and mesenteric lymph nodes; diffuse, chronic nephritis; decubitous ulcerations; callosities over base of the left metatarsal bones; hyperplasia of the testicles; fibrous increase in the thyroid gland; atrophy of the lower extremities with replacement of fatty fibrous tissues; contractures of the feet, both in a spiral with big toe to plantar surface (pes varus et pes equinus) ; slight scoliosis."

The heart muscle showed a slight increase in the interstitial tissue. The recti muscles were nearly normal except that the cross-striations, in some places, were scarcely visible, and some fibers showed a lessened staining capacity. In the gastrocnemii muscles there were only a few normal fibers, as here atrophy was well marked, and the muscular tissue had the appearance of broken bundles of narrow fibers separated by large amounts of fibrous and adipose tissue. In places the muscle fibers were entirely replaced by connective tissue. In other places the muscle bundles had undergone degeneration to such an extent that only the nuclei of the fibers were present. Some fibers that were apparently nearly normal as regards degenerative changes, seemed swollen. An attempt to regenerate the muscle fibers was also observed in a few places. The small arteries in the muscles showed in many instances a diffuse thickening. Organized thrombi were also observed in a few small blood vessels.

The following study of the nervous tissues of this case was commenced in the Neurological Laboratory of the University of Chicago, and completed in the Pathological Laboratory of the State Hospital for Insane, at Independence, Iowa.

VI. HISTO-PATHOLOGICAL EXAMINATION OF THE SPINAL CORD AND THE ROOTS OF THE SPINAL NERVES.

The material here investigated was kindly furnished me by Dr. H. G. Wells, of the University of Chicago.

Sections from different levels of the spinal cord were stained according to the following methods, and a careful histological examination made.

(*a.*) The Marchi Method.—The nerve tissue prepared according to this method had been preserved in formalin and was subsequently treated with Müller's fluid for 20 days, and with an osmic acid mixture for 7 days. After dehydrating in alcohol, the tissue was imbedded in paraffin. Sections were made 20 micra thick, cleared in xylol, and mounted in balsam.

Sections from the following segments of the spinal cord were studied by this method: cervical VIII., lumbar III., IV., V., sacral I. The result of this examination was negative. Only occasionally were nerve fibers found having a black color. We must consequently conclude that in these segments of the cord there was practically no degeneration of nerve fibers.

(*b*) The Iron Hematoxylon Method.—The material studied by this method was preserved in formalin, dehydrated in alcohol, imbedded in celloidin, and sectioned 30 micra thick. After being treated with an ammonio-ferric sulphate mordant, the sections were washed in water and stained with hematoxylon.

Sections prepared according to this method were made from the following segments of the spinal cord: thoracic VI., lumbar III., IV., V. All these sections showed a fairly well marked proliferation of the neuroglia beneath the ependyma of the central canal of the spinal cord. The ependyma was consequently in many places pushed into the central canal in well marked folds. There was also a slight increase in the neuroglia of the gray matter of the spinal cord. Some of the nerve cells have shrunk so that they are surrounded by open spaces and stain rather faintly indicating that chromatolysis has taken place. The blood vessels in the meninges of the spinal cord are seen to be much dilated in several places.

(*c.*) The Nissl Method.—This method is especially servicable in demonstrating the Nissl-bodies, or the tigroid masses in the nerve cell. When the cell body undergoes degeneration, the Nissl bodies usually disintegrate and the cell content becomes more homogeneous than it is normally—in other words, they undergo chromatolysis. The nerve tissue studied by this method was preserved in formalin. It was afterwards fixed still further and dehydrated by alcohol, cleared in cedar oil-xylol and imbedded in paraffin. The sections were made 10 micra thick, stained with Nissl's methylen blue, cleared in oil of cajeput and mounted in colophonium.

The sections studied by this method were from the following segments of the spinal cord: cervical VIII., thoracic VIII., lumbar III., IV., V., and sacral, I., I., III. These show a proliferation of the neuroglia cells around the central canal, as well as the congestion of the blood vessels of the meninges of the spinal cord already mentioned. Chromatolysis of many nerve cells is also evident. This is especially marked in the segments below and including lumbar IV. In these segments there are fewer cells present, especially in the lateral horn, and those present more frequently show chromatolysis. In several instances the nucleus is displaced so as to lie nearer to the periphery of the cell body, and the side of the nuclear membrane nearest to the center of the cell is, in several instances, thickened and wrinkled. The dendrites of the affected cells also shows chromatolysis and have frequently a shrunken appearance.

In concluding the study of the spinal cord of this case of Pseudo-hypertrophic Muscular Atrophy, it is well to keep in mind that this disease is considered one involving primarily the muscles, that lesions in the spinal cord are rarely present, and that when these lesions are present, they are considered secondary or subsequent to the disease of the muscles. The investigation here made substantiates this view except in one respect, viz., the lessened number of lateral horn cells in the segments of the cord below and including lumbar IV., and the frequent chromatolysis of the remaining cells in these segments.

Sano, (1898)[15] has demonstrated that most of the muscles of the leg below the knee are innervated by columns of nerve cells in the lateral horn of the segments of the spinal cord below and including lumbar IV. It is therefore but natural to conclude that the chromatolysis observed, and the possible diminution in the number of cells of the lateral horn of lumbar V, is secondary to the atrophy of the muscles.

Since this patient died from Typhoid Fever it is doubtful if much importance can be given to the other findings,—the proliferation of the neuroglia beneath the ependyma of the central canal of the spinal cord, the slight increase in the neuroglia of the gray matter, and the congested condition of the blood vessels of both the cord and its meninges.

The fact that several of the ventral and lateral horn cells in the lumbar region of the spinal cord had undergone chromatolysis led to the investigation of the roots of the spinal nerves, especially the motor or ventral roots, to determine whether or not these nerve roots contain a smaller number of medullated nerve fibers than do the normal nerve roots. As the author three years ago measured the areas and counted the medullated nerve fibers of both the motor and the sensory nerve roots from the spinal cord of a normal subject, such a comparison becomes possible. According to the author's results, published June, 1903[16], the dorsal or sensory spinal roots of the left side have together an area in cross-section of 54.93 mm^2. and contain 653,627 medullated nerve fibers; and according to the results published in 1904[17], the ventral or motor spinal roots of the left side have together an area in cross-section of 26.50 mm^2. and contain 203,700 medullated nerve fibers. In other words the ratio of the areas of the cross sections of the ventral and dorsal roots is as 1 :2.07, while the ratio of the numbers of medullated nerve fibers is as 1 :3.2. From the author's results similar comparisons can also be made for each pair of nerve roots. The nerve roots investigated were studied both by Marchi's and Pal-Weigert's methods. The Marchi method gave only negative results. The few black droplets present were not sufficiently numerous to indicate much degeneration. But as this was a case of long standing, it is most probable that the disintegrated myelin of the degenerated nerve fibers had disappeared by absorption.

In using the Pal-Weigert method the material was first fixed in formalin, and later in Müller's fluid. It was then washed in water, dehydrated in alcohol and ether, imbedded in celloidin, and sectioned 30 micra thick. The sections were stained in Weigert's hematoxylon, and differentiated with potassium permanganate, oxalic acid, and acid potassium sulphate. After washing in water, dehydrating in alcohol, clearing in creosote, they were mounted in balsam.

In determining the areas of the cross sections of the nerve roots, camera lucida projections were made on millimeter paper, the square millimeters counted, and from these results were calculated the true areas by dividing the results thus obtained by the square of the magnification of the projections. In counting the medullated nerve fibers a Zeiss microscope fitted with a Zeiss objective, 4 mm., aperture 0.95, and oculus No. 6 was used. In the oculus was placed an ocular micrometer ruled into square millimeters. The counting was done by means of an automatic register.

The following table shows a comparison of the areas of the cross sections of the left nerve roots of the spinal cord of a large, normal man, with similar areas from the nerve roots of this small man here reported as suffering from Pseudo-hypertrophic Muscular Atrophy.

	Areas of cross-sections of nerve roots from normal cord.			Areas of cross-sections of nerve roots from abnormal cord.		
	Motor Roots.	Sensory Roots.	Ratio.	Motor Roots.	Sensory Roots.	Ratio.
Lumbar IV.	1.27mm^2	2.93mm^2	1 :2.3	0.47mm^2	1.66mm^2	1 :3.4
V.	2.17 “	3.20 “	1 :1.5	1.28 “	1.99 “	1 :1.6
Sacral I.	1.98 “	3.44 “	1 :1.7	1.49 “	2.34 “	1 :1.6
II.	0.61 “	1.92 “	1 :3.2	0.45 “	1.39 “	1 :3.1

The nerve roots of the lower lumbar and the upper sacral nerves only were investigated as the muscles of the calves of the legs—those most atrophied in this case—are mainly innervated by these nerves. The areas of the cross sections of the nerve roots from the spinal cord of the case here reported are found to be considerably smaller than those from the nerve roots of the normal cord. This is probably partly due to the difference in the sizes of the two subjects.

From the fore-going table it is evident that the ratio between the areas of the cross sections of the motor and sensory roots of the 4th lumbar segment differs in the two cases. The ratio of the normal roots being 1 : 2.3; and that from the roots of the case here reported 1 : 3.4. This is without doubt due to the fact that the motor root (lumbar IV) is smaller that it should be.

To determine whether there is also a corresponding diminution in the number of nerve fibers in these roots a count was made of the nerve fibres in the motor root of the left spinal nerve of the 5th lumbar segment. The result of this count was 5171 nerve fibers as compared with 10,366 in the corresponding normal root. That the different sizes of the two bodies from which the material was obtained partly accounts for this seems evident. This is, however, not the only reason for this difference.

In counting the fibers in the nerve root from the case here reported it was noticed that there were practically no small nerve fibers present. From the author's former investigation (1904) it was determined that the corresponding normal nerve root contains 15% of small fibers (less than 7 micra in diameter). This difference in the number of small nerve fibers in the two roots compared suggest the idea that possibly there was present a diminution in the number of fibers without a corresponding proportionate diminution in the area of the cross section of the nerve root from the case here reported. That this is the case is seen from the fact that the normal root contains, on the average, 4800 nerve fibers per mm^2, while the other root contains on the average 4040. It is therefore evident that the root here investigated not only has a smaller area than the normal root, but contains a smaller number of fibres, as well as, a smaller number of fibers per mm^2.

This diminution in the area of the cross section and in the number of fibers in the root under discussion is without doubt due to a degeneration of some of its nerve fibers and agrees well with the fact already referred to that some of the motor cells of the lateral and ventral horns of the lumbo-sacral segments of the cord were undergoing chromatolysis—some having even disappeared.

Boughton (1906)[18] demonstrated that in the oculomotor nerve of the white rat and of the cat the "small" fibers appear after the period of most rapid growth. This fact suggested the idea that the diminution in the number of small fibers in the roots here studied might be due to the fact that the onset of the muscular atrophy occurred at such an early period as to prevent the normal growth of the "small" nerve fibers.

The fact that the ratios of the cross sections of the motor and sensory roots from the other segments of the cords compared are so nearly equal would seem at first thought to indicate that there was no degenerative process here present. This conclusion is, however, not necessarily correct. As was pointed out above there is evidence of a greater diminution in the number of nerve fibers than in the area of the cross sections of the nerve root investigated. This makes it probable that in the other motor nerve roots of the lumbo-sacral segments there is also present a diminution in the number of nerve fibers.

VII. DIAGNOSIS.

The diagnosis of Pseudo-hypertrophic Muscular Atrophy in this case is based on the following facts:

1. The early onset.—The first symptoms were observed before the child was two years of age. It was apparent to the father that something was wrong with the child's feet and ankles; but this was not sufficiently marked at first to satisfy those who saw the child that the trouble was of a serious nature.

2. The slow progress of the trouble.—The trouble was for sometime unnoticed, and, when sufficiently advanced to be apparent, was observed to grow worse only very gradually. He gradually became emaciated and weak, and died at the age of twenty years from an attack of Typhoid-Fever. During the last days of his illness, a hypostatic pulmonary congestion was present.

3. The calves of the legs first affected.—The first muscles affected were those of the calves of both legs. These at first seemed large to the father, but after a time became thinner than in normal children.

4. The difficulty in walking.—He never learned to walk well, and fell frequently when attempting to walk. This difficulty was due to contractures, described under another heading.

5. The difficulty in arising from a sitting posture.—He invariably found it necessary to use his hands in arising.

6. The characteristic way of arising from the recumbent position.—He would roll over on his stomach, get up on his knees and elbows, then on all fours, and finally by placing his hands on his knees, raise the trunk to the erect position.

7. Contractures and deformity of his feet.—This resulted

first in *pes varus*—the walking on the outer sides of his feet; and later in *pes equinus*—the walking on the balls of the feet and the heel not touching the ground. He was unable to flex his feet dorsally and as the disease advanced, was compelled to use canes and crutches in walking.

8. The scoliosis.—The spinal column showed a fairly well marked lateral curvature.

9. The vaso-motor disturbances in the calves of his legs.—His feet and the calves of his legs were, after the disease had progressed a few years, generally cold and he seemed to have, as might be expected, a lessened sensibility for cold sensations in them.

10. The microscopical examination of the gastrocnemius muscles revealed a condition characteristic of pseudo-hypertrophic atrophy.

11. An apparent disturbance of the function of the rectum.—He experienced an occasional inability to hold the contents of the rectum, especially when he felt the need of evacuating his bowels. Since he felt the need of evacuating his bowels, there may be some doubt that this disturbance is of nervous origin. It is highly probable that his extreme emaciation, and that the local ulceration of the rectum revealed by scars at the post-mortem examination, were responsible for this disturbance of function. The fact that there was no disturbance of the function of the bladder also supports this view.

12. The prominent shoulder-blades.—It is not certain whether this was due to the general emaciation or to an atrophy of the muscles concerned.

. 13. The impaired function of the hands.—This, in all probability, was due to an atrophy of the muscles of the hand—a condition not rare in this disease.

14. The unimpaired intellect.

It is to be regretted that we have no data as to the presence or absence of fibrillary contractions in the affected muscles, as to the condition of the deep reflexes, nor as to the electric reaction of the muscles.

In favor of the diagnosis here made of Pseudo-hypertrophic Muscular Atrophy, and against a possible diagnosis of Acute Poliomyelitis Anterior, is the absence of such characteristic symptoms of the latter disease as:—(1) the fever attack, (2) the acute onset,—sudden paralysis, (3) the partial recovery of the affected muscles, etc.

VIII. CONCLUSION.

1. The most important pathological changes observed in the muscle fibers of the muscles most affected in this case were: cross-striations less marked, lessened staining capacity, pseudo-pertrophy, fatty degeneration, etc. Some of the small blood vessels in the muscles show the diffuse thickening and organized thrombi.

2. The proliferation of the neuroglia beneath the ependyma of the central canal, the slight increase in the neuroglia of the gray matter, and the congested condition of the blood vessels of the spinal cord were probably due to the Typhoid Fever from which the patient died.

3. The chromatolysis of the nerve cells of the gray matter of the cord, especially of the lateral horn, in the segments below and including lumbar IV, is best explained by considering it secondary to the degenerative changes in the muscles.

4. The column of nerve cells in the lateral horn of the lumbo-sacral cord designated No. 7 by Sano[15] seemed to show a diminution in the number of its cell bodies. This was most marked in the 4th and 5th lumbar segments of the cord.

5. The roots of the spinal nerves of the 4th and 5th lumbar and 1st and 2nd sacral segments, both motor and sensory, were found to have a much smaller area of cross-section than those from a normal subject. Thus the area of the cross-section of the left motor root of lumbar IV is only 0.47 mm^2 as compared with 1.27 mm^2 for the normal root. This makes the ratio of the areas of the cross-sections of the motor and sensory roots here studied 1 : 3.4 as compared with 1 : 2.3 for that of the normal roots. This difference in the ratios is due to the abnormal size of the motor root mentioned. The small size of the roots, both motor and sensory, is probably due to several causes,—the material being from a small man, and some nerve fibers having undergone degeneration.

6. The left motor root of the 5th lumbar segment contained by actual count 5,171 medullated nerve fibers as compared with 10,366 for the normal root. In addition to the reasons given for the small areas of the cross-sections of the spinal roots here stud-

ied, it has been suggested that possibly the early onset of this disease prevented the "small" fibers from developing.

7. The muscles most markedly atrophied in this case were those of the calves of the legs—muscles innervated by the cell-bodies of the lateral horns of the lumbo-sacral segments of the spinal cord. This atrophy probably accounts for the chromatolysis of the motor cells referred to, as well as, for the diminution in the number of medullated nerve fibers in the motor roots counted (lumbar V).

8. The histo-pathological findings here reported add support to the conclusion of other investigators that Pseudo-hypertrophic Muscular Atrophy is primarily a disease of the muscles, and that the changes in the spinal cord and in the spinal nerve roots are secondary.

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